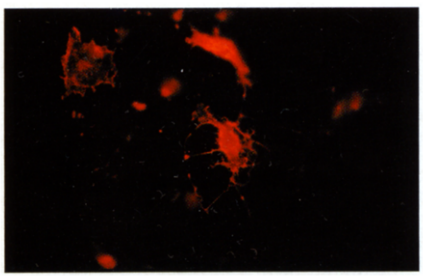
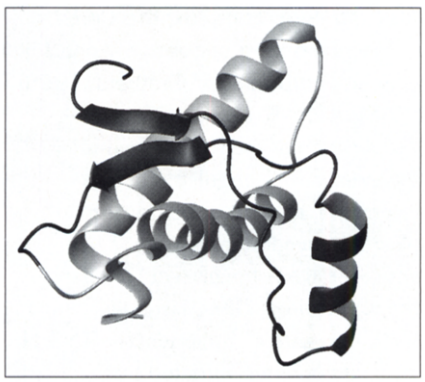


the cell surface. Moreover, SIV seroprevalence and viremia were comparable among CCR5 heterozygotes and wild-type animals. Parallel evolution of CCR5-null alleles in humans and sooty mangabeys suggests that similar negative selection pressures have acted against CCR5, as would occur during epidemics of infectious agents that require CCR5 for pathogenesis. Sooty mangabeys bred to homozygosity for the deletion allele will be useful for experimental studies on the context-dependent role of CCR5 in host defense and microbial pathogenesis.

27 July 1998, Brief Communication, *Current Biology*

☐ **Prion protein fragments spanning helix 1 and both strands of β sheet (residues 125–170) show evidence for predominantly helical propensity by CD and NMR.** Gary J Sharman, Nigel Kenward, Huw E Williams, Michael Landon, R John Mayer and Mark S Searle (1998). *Fold. Des.* **3**, 313–3120.

Transmissible spongiform encephalopathies are a group of neurodegenerative disorders of man and animals that are believed to be caused by an α-helical to β-sheet conformational change in the prion protein, PrP. Recently determined nuclear magnetic resonance (NMR) structures of recombinant PrP (residues 121–231 and 90–231) have identified a short two-stranded anti-parallel β sheet in the normal cellular form of the protein (PrP^C). This β sheet has been suggested to be involved in seeding the conformational transition to the disease-associated form (PrP^{Sc}) via a partially unfolded intermediate state. The authors describe circular dichroism and NMR studies of three peptides (125–170, 142–170 and 156–170) that span the β-sheet and helix 1 region of PrP, forming a large part of the putative PrP^{Sc}–PrP^C binding site that has been proposed to be important for self-seeding replication of PrP^{Sc}. The data suggest that all three peptides in water have predominantly helical propensities, which are enhanced in aqueous methanol. Although the helical propensity is most marked in the region corresponding to helix 1 (144–154), it is also apparent for residues spanning the two β-strand sequences. The authors have attempted to model the conformational properties of a partially unfolded state of PrP using peptide fragments

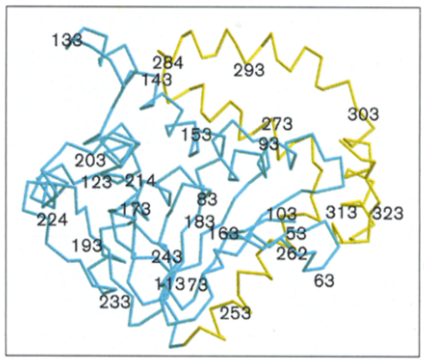


spanning the region 125–170. No evidence was found in the sequence for any intrinsic conformational preference for the formation of extended β-like structure that might be involved in promoting the PrP^C–PrP^{Sc} conformational transition.

8 July 1998, Research Paper, *Folding & Design*

☐ **The crystal structure of dienoyl-CoA isomerase at 1.5 Å resolution reveals the importance of aspartate and glutamate sidechains for catalysis.** Yorgo Modis, Sirpa A Filppula, Dmitri K Novikov, Brian Norledge, J Kalervo Hiltunen and Rik K Wierenga (1998). *Structure* **6**, 957–970.

The degradation of unsaturated fatty acids is vital to all living organisms. Certain unsaturated fatty acids must be catabolized via a pathway auxiliary to

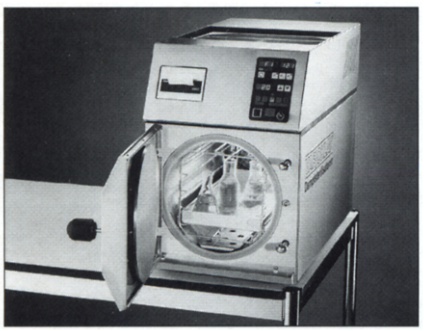


the main β-oxidation pathway. Dienoyl-coenzyme A (dienoyl-CoA) isomerase catalyzes one step of this auxiliary pathway, the isomerization of 3-*trans*, 5-*cis*-dienoyl-CoA to 2-*trans*,4-*trans*-dienoyl-CoA, and is imported into both mitochondria and peroxisomes. Dienoyl-CoA isomerase belongs to a family of CoA-binding proteins that share the enoyl-CoA hydratase/-isomerase sequence motif. The crystal structure of rat dienoyl-CoA isomerase has been determined. The fold closely resembles that of enoyl-CoA hydratase and 4-chlorobenzoyl-CoA dehalogenase. Dienoyl-CoA isomerase forms hexamers made up of two trimers. The structure contains a well ordered peroxisomal targeting signal type-1 that is mostly buried in the inter-trimer space. The active-site pocket is deeply buried and entirely hydrophobic, with the exception of the acidic residues Asp176, Glu196 and Asp204. Site-directed mutagenesis of Asp204 revealed that this residue is essential for catalysis. In a molecular modeling simulation, a molecule of 3-*trans*,5-*cis*-octadienoyl-CoA was docked into the active site. The structural data, supported by the mutagenesis data, suggest a reaction mechanism where Glu196 acts as a proton acceptor and Asp204 acts as a proton donor. In the predicted mode of substrate binding, an oxyanion hole stabilizes the transition state by binding the thioester oxygen. The presence of a buried peroxisomal targeting signal suggests that dienoyl-CoA isomerase is prevented from reaching its hexameric structure in the cytosol.

15 August 1998, Research Paper, *Structure*

Product News

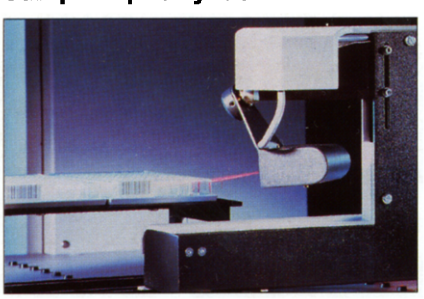
New steam steriliser



The **VARIOKLAV** line of steam sterilisers by **H+P Labortechnik** has now been complemented by the compact benchtop steriliser **250T**. In the development of this smallest member of the VARIOKLAV range, H+P Labortechnik was able to draw on more than 20 years of experience in sterilisation technology. The result is a product that excels in usability and value. The steam atmosphere is efficiently swirled by a novel radial fan that eliminates the need for a shaft exit. The radial fan inside the steriliser chamber is driven by a wear-free drive system located outside the pressure vessel, permitting rapid and even heating, short cooling times, and precision convergence on the sterilisation temperature without overheating sensitive culture media. With a size of only 380 × 650 mm, this steriliser offers excellent space economy, while at the same time its interior chamber height of 24 cm offers sufficient room for one-litre flasks. The condenser unit is fastened onto a swing arm, allowing rapid and effortless cleaning of the reservoir. There are a broad range of expansion options catering to a variety of special requirements, for example a thermolock to protect the operator from scalding when sterilising liquids.

Circle number 1 on reader response card.

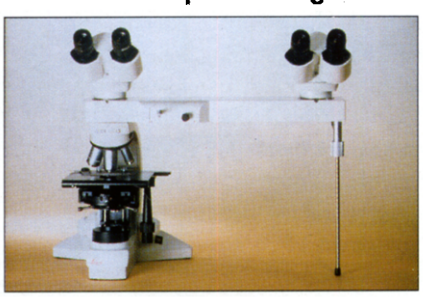
Samples quickly identified



Life sciences laboratories that need to locate potentially interesting samples quickly and easily from master plates or tubes should take a look at the new **Pos-ID** bar code scanner on **TECAN's Genesis RSP** (Robotic Sample Processor). The Pos-ID (version2), which can be upgraded, helps guarantee safe and secure sample preparation or screening. The scanner identifies primary and secondary plates or tubes and tracks their position and orientation on the worktable. Pos-ID can alert users if a tube or microplate container is missing.

Circle number 2 on reader response card.

Dual and multiple viewing

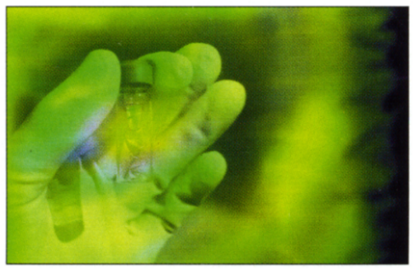


Leica offers a variety of dual and multiple viewing solutions for use on the **Leica DM LS** and **Leica DM LB** laboratory microscope systems. The advanced ergonomic design of the DM LS makes teaching and consultation an easy task. Dedicated dual view bridges for face-to-face orientation allow either microscope stand to easily fit on the return of the desk. For laboratory bench situations or any time the operators must be on the same side of the microscope, the side-by-side bridge offers an alternative solution. The system allows from 3 to 10 viewing stations.

Circle number 3 on reader response card.

In Brief

Fluorescence detection



JBL Scientific, Inc., innovators in alkaline phosphatase substrates, have introduced **AttoPhos Plus™**, a new alk phos substrate generating fluorescent molecules detectable at the attomolar level. AttoPhos Plus™ offers advantages such as detection at lower levels of pH, reduced background, high sensitivity and large Stoke's shift.

Circle number 4 on reader response card.

Enhanced combinatorial synthesis

The new **Combi-Clamp™** from **Whatman** enlarges the universe of reactions available to drug discovery and other chemists who use combinatorial synthesis to generate libraries of compounds for screening. A simple-to-use device, Combi-Clamp™ allows the uses of organic and other highly volatile solvent systems by eliminating the problems associated with evaporation. This allows optimization of reaction times, and conditions that otherwise would be difficult to achieve without a closed system, as well as eliminating loss of sample or solvent due to dripping.

Circle number 5 on reader response card.

High fidelity PCR

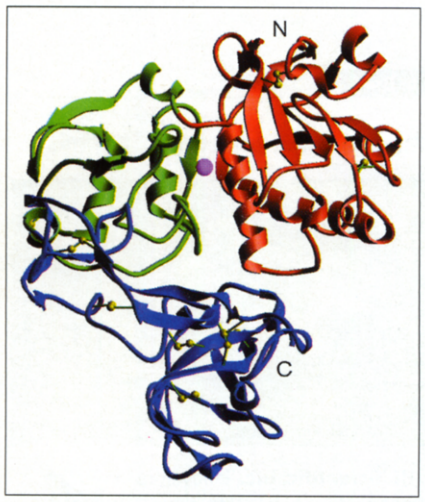
Hybaid has introduced the new **Proof*Sprinter*™** DNA polymerase mix, a licensed enzyme for high yield and high fidelity PCR reactions of up to 20 kb. The mixture combines the proof-reading capacity of *Pwo* with the high processivity of *Taq*, making it the enzyme of choice for cloning or sequencing of PCR products. Proof*Sprinter*™ has robust performance due to high DNA polymerase activity.

Circle number 6 on reader response card.

Software upgrades

Universal Imaging Corporation has introduced versions 3.5 of **MetaMorph**, **MetaFluor** and **MetaGFP**. These packages give scientists and industrial users the power to do advanced microscope automation, acquire and analyze fluorescent and transmitted light images, and find intra-cellular ion measurements using single wavelength or ratio imaging dyes.

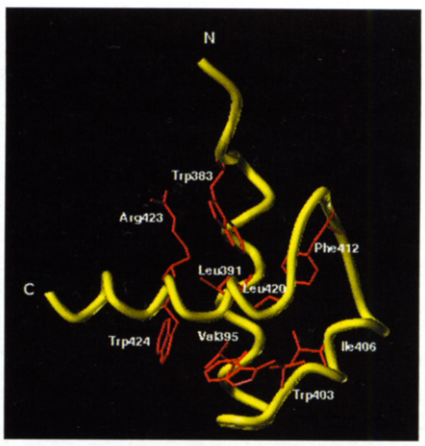
Circle number 7 on reader response card.



more widespread than indicated by sequence homologies amongst existing metzincin zinc proteinases. The similarity of the active-site structure to previously well characterized metzincin class zinc proteinases should aid the development of specific inhibitors. These inhibitors might be used to determine the function of leishmanolysin in the insect and during mammalian infection, and could aid in the development of drugs for human leishmaniasis.
15 August 1998, Research Paper, *Structure*

☐ **Solution structure of the DNA-binding domain of human telomeric protein, hTRF1.** Tadateru Nishikawa, Aritaka Nagadoi, Shoko Yoshimura, Saburo Aimoto and Yoshifumi Nishimura (1998). *Structure* **6**, 1057–1065.

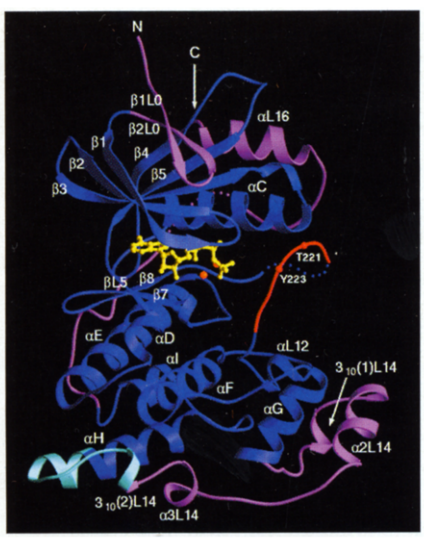
Mammalian telomeres consist of long tandem arrays of the double-stranded TTAGGG sequence motif packaged by a telomere repeat binding factor, TRF1. The DNA-binding domain of TRF1 shows sequence homology to each of three tandem repeats of the DNA-binding domain of the transcriptional activator c-Myb. The isolated c-Myb-like domain of human TRF1 (hTRF1) binds specifically to telomeric DNA as a monomer, in a similar manner to that of homeodomains. So far, the only three-dimensional structure of a telomeric protein to be determined is that of a yeast telomeric protein, Rap1p. The DNA-binding domain of Rap1p contains two subdomains that are structurally closely related to c-Myb repeats. The solution structure of the DNA-binding domain of hTRF1 has been determined and shown to comprise three helices. The architecture of the three helices is very similar to that of each Rap1p



subdomain and also to that of each c-Myb repeat. The hTRF1 DNA-binding domain is likely to bind to DNA in a similar manner to that of the second subdomain of Rap1p. On the basis of the Rap1p–DNA complex, a model of the hTRF1 DNA-binding domain in complex with human telomeric DNA was constructed. In addition to DNA recognition by the HTH variant, a flexible amino-terminal arm of hTRF1 is likely to interact with DNA.
15 August 1998, Research Paper, *Structure*

☐ **Crystal structure of JNK3: a kinase implicated in neuronal apoptosis.** Xiaoling Xie, Yong Gu, Ted Fox, Joyce T Coll, Mark A Fleming, William Markland, Paul R Caron, Keith P Wilson and Michael S-S Su (1997). *Structure* **6**, 983–991.

The c-Jun N-terminal kinases (JNKs) are members of the mitogen-activated protein (MAP) kinase family, and regulate signal transduction in response to environmental stress. Activation and nuclear localization of JNK3, a neuronal-specific isoform of JNK, has been associated with hypoxic and ischemic damage of CA1 neurons in the hippocampus. Knockout mice lacking JNK3 showed reduced apoptosis of hippocampal neurons and reduced seizure induced by kainic acid, a glutamate-receptor agonist. Thus, JNK3

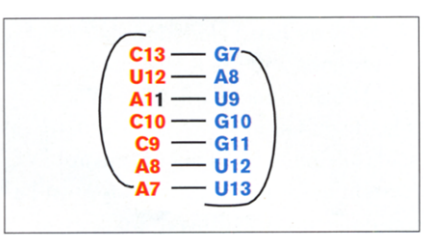


might be important in the pathology of neurological disorders and is of significant medical interest. The authors report here the structure of unphosphorylated JNK3 in complex with adenylyl imidodiphosphate, an ATP analog. In contrast to other known MAP kinase structures, the ATP-binding site of JNK3 is well ordered; the glycine-rich nucleotide-binding sequence forms a β-strand–turn–β-strand structure over the nucleotide. Unphosphorylated JNK3 assumes an open conformation, in which the amino- and carboxyl-terminal domains are twisted apart relative to their positions in cAMP-dependent protein kinase. The rotation leads to the misalignment of some of the catalytic residues. This is the first JNK structure to be determined, providing a unique opportunity to compare structures from the three MAP kinase subfamilies. The structure reveals atomic-level details of the shape of JNK3 and the interactions between the kinase and the nucleotide. The structure provides a framework for understanding the substrate specificity of different JNK isoforms, and should aid the design of selective JNK3 inhibitors.

15 August 1998, Research Paper, *Structure*

☐ **The solution structure of an RNA loop–loop complex: the *ColE1* inverted loop sequence.** Anna J Lee and Donald M Crothers (1998). *Structure* **6**, 993–1005.

Replication of the *ColE1* plasmid of *Escherichia coli* is regulated by the interaction of sense and antisense plasmid-encoded transcripts. The antisense RNA I negatively regulates the replication of the plasmid by duplex formation with complementary RNA II. The interaction is initiated by the formation of a double helix between seven-nucleotide loops from each RNA and is stabilized by binding of the RNA one modulator (ROM) protein. The ROM protein is thought to recognize a specific RNA structure, regardless of sequence. The solution structure of a loop–loop complex between model RNA hairpins that resemble RNA I and RNA II has been determined using nuclear magnetic resonance spectroscopy. The model hairpins have loop sequences inverted 5′ to 3′ relative to the wild-type sequence and were chosen because of their complex's slow dissociation in comparison to the wild



type. The complex has continuous stacking from the 3′-side of one stem helix through the loop–loop helix to the other stem helix. One residue from each hairpin has a unique phosphodiester bond which bridges and narrows the major groove. These bridging phosphates are in close proximity to the phosphate groups of the adjacent bases, forming unique structural motifs called phosphate clusters. Unique distortions, such as the strong bend and the phosphate clusters flanking the major groove of the loop–loop helix, provide an attractive nonsequence-specific structural feature for recognition by the ROM protein. The structure provides a basis for rationalizing the sequence dependence of the stability of loop–loop interaction.

15 August 1998, Research Paper, *Structure*

☐ **The crystal structure of the *Leishmania major* surface proteinase leishmanolysin (gp63).** Edith Schlagenhauf, Robert Etges and Peter Metcalfors (1998). *Structure* **6**, 1035–1046.

Despite their medical importance, there is little available structural information for the surface antigens of infectious protozoa. Diseases caused by the protozoan parasite *Leishmania* are common in many developing countries. Human infection occurs during the bite of infected sandflies, when *Leishmania* promastigote cells from the insect gut enter the bloodstream. Promastigotes in the blood parasitize macrophages, often causing serious disease. Leishmanolysin is the predominant protein surface antigen of promastigotes, and is assumed to have a key role during infection. Leishmanolysin is a membrane-bound zinc proteinase, active *in situ*. Similar molecules exist in other trypanomastid protozoa. Two crystal forms of leishmanolysin were obtained from protein purified from promastigote membranes. The structure clearly shows that leishmanolysin is a member of the metzincin class of zinc proteinases. The unexpected metzincin features of the leishmanolysin structure suggest that the metzincin fold might be